中文題目：邊緣區型淋巴癌以類似多發性骨髓瘤之表現復發

英文題目：Recurrent marginal zone lymphoma with bone marrow involvement mimicking myeloma

作　　者：葉宗讓[1]，蕭惠樺[1, 2]

服務單位：[1]高雄醫學大學附設醫院內科部血液腫瘤科，[2]高雄醫學大學

Introduction

Multiple myeloma is a unique malignant disease which presents neoplastic proliferation of plasma cells producing a monoclonal immunoglobulin with typical CRAB (hypercalcemia, renal failure, anemia and bone lesions) presentation. Increased plasma cell in noticed in most of these cases. However, some lymphoma with bone marrow involvement could mimic myeloma. The disease presentation, serologic finding and plasma cell-like morphology could be very similar and so differential diagnosis could be challenging. Here, we present a case of recurrent marginal zone lymphoma with bone marrow involvement mimicking myeloma

Case presentation

A 60-year-old with past medical history of thalassemia and hypertension. He was diagnosed with left ankle marginal zone lymphoma, Ann Arbor stage IE, in 2013. Local radiotherapy (total with 30Gy) was performed for lymphoma treatment. After that, he followed at Hematology OPD regularly. In December, 2018, progressive dyspnea presented. He denied B-symptoms (fevers, chills or night sweats). Chest X-ray showed left side pleural effusion. Thoracentesis followed by chest CT were performed for evaluation. Effusion analysis revealed exudate with lymphocyte predominate. Many mono- or multinucleate abnormal cells with variable N/C ratio and perinuclear halo were seen. There was a highly elevated IgA of 6180 mg/dL, decreased IgG of 479 mg/dL, decreased IgM of 49.5 mg/dL, free kappa 26.1 mg/L and free lambda 7.6 mg/L with a kappa/lambda ratio of 3.43. Serum protein electrophoresis showed monoclonal peak at beta region with A/G ratio reverse (0.36). Serum immunofixation confirmed an extra monoclonal band being IgA / Kappa identity. Urine immunofixation showed biclonal immunoglobulins (one IgAκ and one kappa light chain). Bone marrow smear showed abundant plasma-cell like cells. Multiple myeloma was favored initially. However, further examination showed different diagnosis. Bone marrow immunophenotying done by flow cytometry showed abnormal B-lymphocyte population The chromosomal abnormality of 46, XY, t(14;18)(q32;q21) was detected. Cell clonality confirmed the same clone B-cell from previous marginal zone lymphoma. According to above information, the diagnosis of recurrent marginal zone lymphoma with plasmacytic differentiation with bone marrow involvement is made.

Discussion

Marginal zone is the outer part of the mantle zone of B-cell follicles. Post-germinal center memory B cells present in the marginal zone. Marginal zone lymphoma (MZL) refers to a group of indolent B-cell lymphomas that originate from the marginal zone of lymphoid follicles.[2] MZL comprised three different entities, extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma), the nodal marginal zone lymphoma and the splenic marginal

zone lymphoma. These tree subtypes share similar morphological and immunophenotypic features but they have distinct epidemiologic, pathologic and molecular features. The relative frequency of MZL is 7.7% in developing regions and 11.7% in developed regions (North America and Western Europe) from the International Non-Hodgkin Lymphoma Classification Project in 4539 cases between 1995 and 2012.[3] The most common subtype is extranodal MZL, which may occur in many different anatomic locations and the gastrointestinal tract is the most common site. Disseminated disease appears to be more common in non-GI MALT lymphomas.[4] Typical MZL cell express surface immunoglobulins and pan-B antigens (CD19, CD20, and CD79a), express the marginal zone-associated antigens CD35 and CD21, and lack CD5, CD10, CD23, and cyclin D1 expression. [1] The common karyotypic alterations that characterize MALT lymphomas include the trisomies 3 and 18, the translocations t(11;18)(q21;q21), t(1;14)(p22;q32), t(14;18)(q32;q21), t(3;14)(q27;q32), and t(3;14)(p14.1;q32). [5]

In this patient, due to the increased plasma cell-like cells in bone marrow with significant monoclonal gammopathy (IgAκ), plasma cell disorders are favored initially. However, abnormal B-lymphocyte population other than plasma cell were noticed from bone marrow flow cytometric immunophenotyping. Adding to patient's marginal zone lymphoma history, recurrent lymphoma with bone marrow involvement was impressed. Further supporting information were same cell clonality, comparing current abnormal B-lymphocyte with his initial MZL cells in 2013, and the common MZL karyotypic alternation, t(14;18)(q32;q21).

In MALT lymphoma, plasmacytic differentiation is found in approximately one third of cases.[6] Theoretically, B lymphocytes undergo plasmacytic differentiation only after leaving germinal center. However, almost all small B lymphoid neoplasms may present this phenomenon, including chronic lymphocytic leukemia/small lymphocytic lymphoma, follicular lymphoma and mantle cell lymphoma. It could vary from being uniformly present (as in lymphoplasmacytic lymphoma) to very uncommon (as in mantle cell lymphomas).[7] Therefore, the diagnosis relying heavily on the characterization of the lymphoid component, including phenotypic, cytogenetic/molecular, and sometimes clinical findings. [7] As the development of gene mutational analysis, the detection of some special mutation could have a huge impact on the diagnosis, such as *MYD88* L265P mutation. *MYD88* L265P mutations are in the vast majority of lymphoplasmacytic lymphomas (LPLs) / Waldenström macroglobulinemia. It could be used to different diagnosis LPL from other lymphoma with plasmacytic differentiation. However, not all hospitals could perform testing for *MYD88* mutations in Taiwan currently. As the result, using other method to differential diagnosis is crucial, just like the case we presented.